McDermott
Will & Emery

# New Law Extends Federal Oversight of Compounding Pharmacies, Establishes National Drug Track-and-Trace Requirements

January 22, 2014

On November 27, 2013, President Obama signed the Drug Quality and Security Act (the Act) (Public Law No. 113-54) into law. The Act addresses two hot-button issues relating to marketed drug products: the extent of federal oversight of compounding pharmacies, and the establishment of a long-sought uniform national drug track-and-trace system.

## Oversight of Compounding Pharmacies

The Act establishes an optional program that allows pharmacy compounders to voluntarily subject themselves to federal oversight by registering as an "outsourcing facility." An "outsourcing facility" is a facility, geographic location or address that is engaged in the compounding of sterile drugs, has elected to register with the U.S. Food and Drug Administration (FDA) as an outsourcing facility, and has complied with the requirements of the Act.

*Outsourcing Facility Requirements*

The Act's requirements for outsourcing facilities include the following:

- **Registration.** Outsourcing facilities must register annually.

- **Drug reporting.** Outsourcing facilities must, on a biannual basis, submit a list of drugs compounded by the facility during the previous six-month period. Required information for each drug includes active ingredient, source of active ingredient, National Drug Code (NDC) of source drug or bulk active ingredient, dosage form, route of administration, package description and number of individual units (among other items).

- **Electronic submission of information.** Outsourcing facilities must submit registration and drug reporting information electronically unless the FDA grants a request for waiver.

- **Labeling.** Outsourcing facilities must include the following information in the drug labeling: the statement "This is a compounded drug" or a reasonable comparable alternative statement; the name, address and phone number of the outsourcing facility; and, with respect to the drug itself, the lot or batch number, established name, dosage form and strength, a list of active and inactive ingredients, a statement of quantity or volume, the date the drug was compounded, expiration date, storage and handling instructions, NDC number, the statement "Not for resale," and, if the drug is dispensed or distributed other than pursuant to a prescription for an individual identified patient, the statement "Office Use Only."

- **Adverse event reporting.** Outsourcing facilities must submit adverse event reports in accordance with the requirements for non-compounded new drugs.

- **Prohibition on wholesaling.** A drug compounded by an outsourcing facility may not be sold or transferred by an entity other than the outsourcing facility that compounded the drug.

- **Risk-based inspections.** Outsourcing facilities must submit to inspection by the FDA. Risk factors the FDA will consider for inspection include the compliance history of the facility; the record, history and nature of recalls linked to the facility; the inherent risk of the drugs compounded at the facility; the inspection frequency and history of the facility, including whether the facility has been inspected within the last four years; and whether the facility has registered as an entity that intends to compound a drug that presents demonstrable difficulties for compounding.

- **Establishment and re-inspection fees.** Outsourcing facilities must pay an annual establishment fee (payable at the time of registration) and a re-inspection fee (if subject to re-inspection, payable after the FDA has conducted the re-inspection). The cost of registration and any individual re-inspection is $15,000, adjusted annually for inflation. Small businesses (*i.e.*, those with $1 million or less in gross annual sales) are entitled to pay at a discounted rate (one-third of the amount(s) calculated as described above). If an outsourcing facility fails to pay its registration and/or re-inspection fees, respectively, the drugs produced by the facility shall be considered misbranded until such fees are paid.

If a drug is compounded by or under the direct supervision of a licensed pharmacist in a facility that elects to register as an outsourcing facility, the compounded drug will be exempt from the FDA's new drug and adequate-directions-for-use requirements, as well as the new track-and-trace requirements (summarized below). Notwithstanding a compounding pharmacy's status as an outsourcing facility, the Act prohibits the resale of a compounded drug that is marked "not for resale" and the

intentional falsification of a prescription. The Act also specifies that a compounded drug shall be considered misbranded if its advertising or promotion is false or misleading in any particular.

*Requirements for FDA*

The Act requires the FDA to take several steps to implement the "outsourcing facility" program. In addition to the steps implicit in the requirements listed above, the agency must take the following actions:

- **Establish an online list of each facility registered as an outsourcing facility.** The FDA shall post on its website a list of the name of each facility, the state in which the facility is located, whether the facility compounds from bulk drug substances, and whether any such compounding from bulk drug substances is for sterile or non-sterile drugs.

- **Create a list of drugs that present "demonstrable difficulties for compounding."** The FDA is required to establish—via regulation—a list of drugs that present demonstrable difficulties for compounding and are reasonably likely to lead to an adverse effect on the safety or effectiveness of the drug or category of drugs, taking into account the risks and benefits to patients. The FDA must consult with an advisory committee on compounding prior to issuing this regulation. The FDA also must review this list and update it as necessary at least once every four years.

- **Establish a list of bulk drug substances for which there is clinical need.** An outsourcing facility is not permitted to compound using bulk drug substances unless the bulk drug substance appears on a list established by the FDA that identifies bulk drug substances for which there is clinical need (among other exceptions). This list shall be established via notice and comment rulemaking.

- **Submit an annual report to Congress regarding fees collected and assessed under the outsourcing facility program.** This report must be submitted no later than 120 days after each fiscal year in which fees are assessed and collected. The report should include, among other things, a description of fees assessed and collected; a summary description of the entities paying the fees; a description of the hiring and placement of new staff; a description of the use of fee resources to support inspections; and the number of inspections/re-inspections performed each year.

- **Establish implementing regulations via notice and comment rulemaking.** Insofar as the FDA issues regulations implementing this new system, it must issue a notice of proposed rulemaking that includes the proposed regulation, provide a period of at least 60 calendar days for comments on the proposed regulation, and publish the final regulation within 18 months following publication of the proposed rule and at least 30 calendar days before the effective date of the final regulation.

- **Communicate with state boards of pharmacy.** The FDA must receive submissions from state boards of pharmacy describing actions taken against compounding pharmacies or expressing concerns that a compounding pharmacy may be acting contrary to federal law. In turn, the FDA must immediately notify state boards of pharmacy if it receives a submission from another state board of pharmacy, or if the FDA makes a determination that a compounding pharmacy has acted contrary to federal law.

*Implications*

The Act extends federal oversight of pharmacy compounding to the extent that an individual compounding pharmacy wishes to affirmatively subject itself to federal regulatory oversight. Because participation in the outsourcing pharmacy program is strictly voluntary, the new law, at least initially, may affect oversight of compounding pharmacies on a broader scale only if the purchasers of compounded drugs—*e.g.*, hospitals, physicians—require compounders to submit to federal oversight under this program. Notwithstanding the FDA's recent call for entities that purchase compounded drugs to do so solely from entities enrolled in the federal scheme, it remains to be seen whether market forces alone will cause compounders to enroll in the program.

It also remains to be seen what effect, if any, the evolving development of the outsourcing pharmacy program will have on government or private insurance payer policies, and whether and how the FDA may, over time, seek to subject compounding pharmacies that do not choose to participate in the program, as well as office-use compounders, to current good manufacturing practice requirements developed under the program. Likewise, it remains to be seen how the FDA and individual states will

address the potential interplay between federal and state regulation when an outsourcing facility compounds drugs for individual patients pursuant to an individual prescription and for a broader patient population.

Notwithstanding the above, the agency clearly has made the rollout of this program a top priority. Since the enactment of the statute, the agency has taken the following actions:

- Issued two draft guidance documents ("Registration for Human Drug Compounding Outsourcing Facilities under Section 503B of the Federal Food, Drug and Cosmetic Act" and "Interim Product Reporting for Human Drug Compounding Outsourcing Facilities under Section 503B of the Federal Food, Drug and Cosmetic Act")
- Requested nominations for the list of drug products that present demonstrable difficulties for compounding
- Requested nominations for a list of bulk drug substances that may be used to compound drug products in outsourcing facilities
- Requested nominations for voting members, non-voting industry representatives and a voting consumer representative for the Pharmacy Compounding Advisory Committee

Interested stakeholders and entities should review these documents and consider submitting comments, as appropriate.

## Requirements for Drug Supply Chain Security

The Act also establishes a series of requirements for drug manufacturers, wholesale drug distributors, dispensers, repackagers and/or third-party logistics providers, respectively, that are intended to create a uniform national drug tracking and tracing system. While the Act sets forth these requirements at a high level, it leaves to future FDA rulemaking and guidance development the task and responsibility of defining the specifics of this overall system.

Thus, the new system is to be phased in gradually over the next 10 years, and the effective date of any individual provision depends on the nature of the provision itself and on the entity or entities to which it applies. This *White Paper* provides an initial overview of the system's requirements without reference to effective dates, followed by a detailed timeline of events for implementation of the system.

*Requirements for Industry and Scope of Law*

Key provisions include the following:

- **Provision, maintenance and/or acceptance of certain information regarding product transactions.** Prior to or at the time of virtually any transaction in which the ownership of a drug product is transferred (except for transfers to a patient), the transferor must provide, and the transferee must accept, transaction history, transaction information and a transaction statement:
    - *Transaction history* is a statement, in paper or electronic form, that includes the transaction information for each prior transaction going back to the manufacturer of the product.
    - *Transaction information* includes the product's proprietary or established name, strength, dosage form, NDC number, container size, number of containers, lot number, the date of the transaction, date of shipment (if more than 24 hours after the date of the transaction), the business name and address of the person from whom ownership is being transferred, and the business name and address of the person to whom ownership is being transferred.
    - *Transaction statement* is a statement, in paper or electronic form, that the entity transferring ownership in the transaction (a) is authorized (*i.e.*, has the appropriate license or registration) under the Act, (b) received the product from a person that is authorized under the Act, (c) received transaction information and a transaction statement from the prior owner of the product, (d) did not knowingly ship a suspect or illegitimate product, (e) has systems and

processes in place to comply with verification requirements, (f) did not knowingly provide false transaction information and (g) did not knowingly alter the transaction history.

- **Attachment of product identifiers to each package and homogenous case of product.** With the exception of items grandfathered under the Act, manufacturers and repackagers must affix or imprint, and wholesale distributors and dispensers may only engage in transactions involving a drug product with, a "product identifier" on each package and homogenous case. A "product identifier" is a standardized graphic that includes, in both human- and machine-readable form, the standardized numerical identifier, lot number and expiration date of the product.

- **Implementation of systems to investigate suspect products and address illegitimate products.** Manufacturers, wholesale distributors, dispensers and repackagers must have systems in place that (a) allow for the investigation and quarantine of suspect product, (b) facilitate a prompt investigation as to whether a suspect product is illegitimate, (c) facilitate the quarantine and disposition of illegitimate product, and (d) notify the FDA and immediate trading partners of illegitimate product.

- **Response to request for verification.** Upon receiving a request for verification, a manufacturer or repackager must, within a reasonable period of time (as determined by the FDA), notify the requestor whether the product identifier that is the subject of the request corresponds to the product identifier affixed or imprinted by the manufacturer. If the manufacturer or repackager identifies a product identifier that does not correspond to that affixed or imprinted by the manufacturer or repackager, the manufacturer or repackager shall treat such product as a suspect product and conduct an investigation. If the manufacturer or repackager has reason to believe that the product is an illegitimate product, the manufacturer or repackager shall advise the person making the request of this belief at the time of its response.

- **Verification prior to further distribution of returned product.** Upon receipt of a returned product that a manufacturer, wholesale distributor or repackager intends to further distribute, the manufacturer, wholesale distributor or repackager must verify the product identifier for the product for each sealed homogenous case of returned product, or, if the product is not in a sealed homogenous case, for each package, before further distributing such product.

- **Prohibition on transactions with "unauthorized" trading partners.** Manufacturers, wholesale distributors, dispensers and repackagers, respectively, may only participate in transactions with "authorized" trading partners. Manufacturers and repackagers are "authorized" insofar as they comply with the FDA's establishment registration requirements; wholesale distributors and third-party logistics providers are "authorized" insofar as they have a valid license under federal or state law and comply with federal reporting requirements; and dispensers are authorized insofar as they have a valid license under state law.

- **Provision of transaction documentation within reasonable time following request by federal or state official.** Upon the request of the FDA or other appropriate federal or state official, in the event of a drug recall or for the purpose of investigating a suspect product or an illegitimate product, manufacturers, wholesale distributors, dispensers and repackagers must provide the applicable transaction information, transaction history and transaction statement within a "reasonable" period of time (as determined by the FDA) after receiving the request.

- **Implementation of package-level tracing requirements.** Once the new system is fully implemented, the transaction information and transaction statements required under the Act must be exchanged in a secure, interoperable, electronic manner. Transaction information shall include a package-level identifier, and regulated entities must have systems and processes in place to verify product at the package level (among other requirements).

- **Compliance with national standards for prescription drug wholesale distributors and third-party logistics providers.** These standards shall apply to all state and federal licenses and shall address the storage and handling of prescription drugs, performance of background checks, *etc.*

- **Preemption of state and local requirements.** The Act expressly preempts state and local requirements for tracing products through the distribution system that are inconsistent with, more stringent than, or in addition to the federal requirements. The Act similarly preempts state and local licensure provisions for wholesale distributors and third-party logistics providers, respectively.

*Requirements for FDA*

The FDA must take several steps to implement the track-and-trace system. In addition to the steps implicit in the requirements listed above, the agency must take the following steps:

- **Required publication of guidance documents.** The FDA must publish a series of guidance documents to aid in implementing the requirements of the Act, including guidance on standards for interoperable exchange of transaction information, transaction history and transaction statements; guidance to aid trading partners in the identification of suspect product and notification termination; guidance that outlines and makes recommendations with respect to the system attributes necessary to secure tracing at the package level; and guidance on processes pursuant to which certain requirements of the Act may be waived (see also discussion of guidance document relating to the establishment of waiver process, below).

- **Provision of opportunities for public participation in development of guidance documents.** In developing guidance documents implementing the requirements of the Act, the FDA must post draft guidance documents online, accept public comments and/or hold a public meeting (or meetings) before issuing final guidance.

- **Establishment of a waiver process for certain requirements.** The FDA must establish a process pursuant to which an entity may apply for a waiver of any requirement set forth in the Act (a) if such requirement(s) would result in undue economic hardship, (b) for emergency medical reasons, or (c) if a product is packaged in a container too small or otherwise unable to accommodate the required product identifier. Via guidance document, the FDA also shall specify whether and under which circumstances a product that is in the pharmaceutical distribution supply chain on the effective date of the product identifier requirement shall be exempt from such requirement. The FDA also is required to establish a process under which it may determine that other products or transactions shall be exempt from the Act's requirements.

The following table provides a timeline of events for the implementation of the new system.

| Effective Date | Required Activity |
|---|---|
| Date of enactment (November 27, 2013) | ▪ State laws are preempted to the extent that they are inconsistent with, more stringent than, or in addition to federal requirements.<br>▪ State requirements for wholesale distributors and third-party logistics providers are preempted if inconsistent with, more stringent than, or in addition to federal requirements. |
| 180 days after date of enactment (May 26, 2014) | ▪ **FDA** issues guidance to aid trading partners in the identification of suspect product and notification termination. |
| One year after date of enactment (November 27, 2014) | ▪ **FDA** issues draft guidance that establishes standards for the interoperable exchange of transaction information, transaction history and transaction statements.<br>▪ **FDA** may begin holding first of at least five public meetings regarding topics necessary to inform issuance of guidance. Within 18 months of conducting a public meeting on (a) unit level tracing and (b) interoperable data exchange, FDA shall issue final guidance; guidance becomes effective no earlier than one year from the date of issuance.<br>▪ **Third-party logistics provider** must report to FDA (a) the state in which the facility is licensed, (b) the identification number of such license, and (c) the name and address of the facility and all trade names under which the facility conducts business. |

| Effective Date | Required Activity |
|---|---|
| January 1, 2015 | ▪ **Manufacturer** must, prior to or at the time of transfer of ownership, (a) provide the subsequent owner with transaction history, transaction information and a transaction statement in a single document (in any paper or electronic format); (b) capture transaction information (including lot-level information), transaction history and a transaction statement for each transaction; and (c) maintain the information, history and statement for at least six years from the date of the transaction.<br>▪ **Manufacturer** may trade only with authorized trading partners.<br>▪ **Manufacturer** must have product verification system in place.<br>▪ **Wholesale distributor** (a) shall not accept ownership of a product unless the previous owner (prior to or at the time of the transaction) provides transaction history, information and statement; (b) shall provide transaction information, history and statement to a subsequent purchaser; and (c) shall capture the transaction history, information and statement for each transaction and maintain for at least six years.<br>▪ **Wholesale distributor** may trade only with authorized trading partners.<br>▪ **Wholesale distributor** must have product verification system in place.<br>▪ **Wholesale distributor** must report (a) each state in which it is licensed (and the appropriate identification number); (b) name/address/contact information for each facility, and all trade names under which the facility operates; and (c) any disciplinary action taken against the wholesale distributor by the federal or state government.<br>▪ **Dispenser** may trade only with authorized trading partners.<br>▪ **Dispenser** must have product verification system in place.<br>▪ **Repackager** (a) shall not accept ownership of a product unless the previous owner, prior to or at the time of the transaction, provides transaction history, information and statement; (b) shall, prior to or at the time of the transaction, provide a subsequent owner with the transaction history, information and statement; and (c) shall capture the transaction information, history and statement for each transaction and maintain such information for at least six years.<br>▪ **Repackager** may trade only with authorized trading partners.<br>▪ **Repackager** shall have product verification system in place.<br>▪ **FDA** shall establish a database of authorized wholesale distributors. |

| Effective Date | Required Activity |
|---|---|
| July 1, 2015 | ▪ **Dispenser** shall not accept ownership of a product unless the previous owner (prior to or at the time of the transaction) provides transaction history, information and statement. When the dispenser transfers ownership of the product (other than dispensing to a patient or returns), it must provide the subsequent owner with transaction history, information and statement (except for sales from one dispenser to another to fill a specific patient need), and shall capture transaction information, history and statements and maintain for at least six years. |
| Two years after date of enactment (November 27, 2015) | ▪ **FDA** shall, by guidance, (a) establish a process where an authorized manufacturer, repackager, wholesale distributor or dispenser may request a waiver from the requirements of the Act if complying with such requirements would cause undue economic hardship; (b) establish a process for determining when a manufacturer or repackager may request an exception to the product identifier requirement if a product is packaged in a container that is too small or that is otherwise unable to bear the required information; and (c) establish a process under which the FDA may decide a product or transaction is exempt from the requirements of the Act.<br>▪ **FDA** shall issue guidance specifying whether and under what circumstances a product that is not labeled with a product identifier but is in the pharmaceutical supply chain on the effective date of the product identifier requirement shall be exempt from the requirements of the Act.<br>▪ **FDA** shall issue regulations regarding standards for licensing wholesale distributors.<br>▪ **FDA** shall issue regulations regarding standards for licensing third-party logistics providers. |
| Four years after date of enactment (November 27, 2017) | ▪ **Manufacturer** must provide transaction information, history and statement electronically unless exception applies (e.g., to a licensed health care practitioner who is authorized to prescribe medication).<br>▪ **Manufacturer** must affix a product identifier to each package and homogenous case of product, and must maintain product identifier information on file for at least six years.<br>▪ **Manufacturer** must have systems in place that allow it to verify products at the package level.<br>▪ **Manufacturer** must respond to a request for verification within reasonable time (as determined by the FDA).<br>▪ **Manufacturer** must verify the product identifier upon receipt of a returned product that the manufacturer intends to re-sell.<br>▪ Until deadline, **dispenser** shall be granted additional time, as necessary, to provide lot-level information that was provided in paper format in response to a request for such information. |
| Five years after date of enactment (November 27, | ▪ **Repackager** must affix a product identifier on each package and homogenous case |

| Effective Date | Required Activity |
|---|---|
| 2018) | of product, and must maintain product identifier information for at least six years.<br>▪ **Repackager** may only engage in transaction if the product has a product identifier (unless product is grandfathered).<br>▪ **Repackager** must maintain records that allow the repackager to associate the product identifier it imprints on a package with the product identifier imprinted by the original manufacturer for at least six years.<br>▪ **Repackager** must be able to verify products at the package level.<br>▪ **Repackager** must respond to verification request within a reasonable amount of time (as determined by the FDA).<br>▪ **Repackager** must verify the product identifier upon receipt of a returned product that the repackager intends to re-sell. |
| Six years after date of enactment (November 27, 2019) | ▪ **Wholesale distributor** may, for saleable returns, accept returned product from dispenser or repackager only if the wholesale distributor can associate returned product with transaction information and transaction statement associated with that product (for all transactions after that date, transaction history shall begin with the wholesale distributor that accepted and verified the returned product).<br>▪ **Wholesale distributor** may engage in a transaction only if the product is encoded with a product identifier (with the exception of grandfathered items).<br>▪ **Wholesale distributor**, on receipt of a returned product that it intends to resell and before further distributing the product, shall verify the product identifier for each homogenized case of the product or on each package. |
| Seven years after date of enactment (November 27, 2020) | ▪ **Dispenser** may engage in a transaction involving a product only if the product is encoded with a product identifier.<br>▪ **Dispenser** verification system must include ability to (a) verify whether the lot number of a suspect product corresponds with the lot number for such product, and (b) verify that the product identifier (of at least three packages or 10 percent of suspect product, whichever is greater, or all packages if there are fewer than three packages) corresponds with the product identifier. |
| 8.5 years after date of enactment (~May 27, 2022) | ▪ **Private independent consultant** issues report about feasibility of interoperable/electronic tracing requirements for dispensers with 25 or fewer employees. |
| 180 days after receiving final consultant assessment (~November 23, 2022) | ▪ **FDA** holds a public meeting at which stakeholders may comment on the private independent consultant's report. |
| 10 years after date of | ▪ Interoperable, electronic tracing requirements go into effect (*i.e.*, transaction |

| Effective Date | Required Activity |
|---|---|
| enactment (November 27, 2023) | information/statements must be exchanged in a secure, interoperable, electronic manner in accordance with standards set forth in guidance). Transaction information must include the package-level product identifier. Entities must establish the systems and processes necessary to verify the product at the product level, to respond to requests for information from the FDA, and to produce the transaction information required going back to the manufacturer.<br>▪ The requirements for provision and receipt of transaction history, the requirements for returns and the requirements as applied to lot-level information expire.<br>▪ Entities must respond to a federal or state request for information within 24 hours of receiving the request (or other reasonable time as determined by the FDA). |

*Implications*

Many states and individual stakeholder entities have long sought a uniform national track-and-trace regulatory set of standards to avoid the logistical and economic difficulty of developing or complying with varying standards—whether state versus federal or among different states—for drug product distributed in interstate commerce. The new legislation provides for the implementation of such a national standard. From an operational standpoint, the Act imposes substantial new drug track-and-trace requirements for drug manufacturers, wholesale distributors, dispensers, repackagers and third-party logistics providers, and is likely to require substantial revisions or upgrades in internal systems and personnel in order to facilitate compliance. However, perhaps in recognition of the complexity of implementing a uniform national system involving numerous supply chain entities, the many day-to-day, operational issues that will need to be fleshed out in regulations and/or guidance documents will occur gradually over a 10-year period under the legislation.

Given the legislation's significant operational impact on the distribution and sale of drug products, all regulated entities involved in the manufacture and sale of drug products should review their current track-and-trace systems and their commercial drug distribution contracts, and carefully monitor future FDA communications regarding implementation of the new system and requirements. There will be numerous opportunities to participate in the development of new regulations and guidance through public meetings and public comment periods, for example, and stakeholders interested in influencing the development of the new requirements should be on the lookout for forthcoming announcements from the agency.

For more information, please contact your regular McDermott lawyer, or:

**James S. Cohen:** +1 202 756 8276 jscohen@mwe.com

**Glenn Engelmann:** +1 202 756 8388 gengelmann@mwe.com

**Michael W. Ryan:** +1 202 756 8088 mryan@mwe.com

For more information about McDermott Will & Emery visit www.mwe.com